



Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Multiple brown tumors with primary hyperparathyroidism mimicking bone metastases [1]

Quy X. Ngo^a, Duy Q. Ngo^a, Toan D. Tran^a, Duong T. Le^{a,*}, Giap N. Hoang^b, Quang V. Le^{a,b}

^a Department of Head and Neck Surgery, Vietnam National Cancer Hospital, 30 Cau Buou Street, Thanh Tri District, Hanoi, Viet Nam

^b Hanoi Medical University, 01 Ton That Tung Street, Dong Da District, Hanoi, Viet Nam

ARTICLE INFO

Article history:

Received 28 November 2020

Received in revised form

31 December 2020

Accepted 1 January 2021

Available online 18 January 2021

Keywords:

Brown tumor

Primary hyperparathyroidism

Bone metastase

ABSTRACT

Multiple osteolytic lesions are usually associated with bone metastasis. However, brown tumor should also be included in the differential diagnosis. Brown tumor is a rare benign lesions in skeletal system, encountered in patients with uncontrolled primary or secondary hyperparathyroidism. In our case report, we present a 35-year-old female with multifocal brown tumor that difficulty in differential diagnosis of metastasis of malignant parathyroid. Additionally, the treatment and follow up after parathyroidectomy are also emphasized.

METHODS: The SCARE 2020 Guideline [1].

© 2021 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction and importance

Brown tumor (BT) is a rare bony benign lesion caused by excess osteoclast activity and hemosiderin deposition as a result of uncontrolled primary or secondary hyperparathyroidism (HPT). This tumor-like lesion can be multifocal and located in any part of the skeleton, but most frequently arises in the jaws, ribs, clavicles, extremities, and pelvic girdle [2,3]. The tumor has similar characteristics to bone cancer metastases on scintigraphy, a highly sensitive screening tool commonly used in oncology [4,5]. The presence of multiple brown tumors is an extremely rare complication of primary HPT (PHPT) with the incidence reported recently as 1% [6], in contrast with the 13% of BT with secondary HPT (SHPT) [7]. We present a case of a 35-year-old woman with multifocal BTs caused by PHPT, mimicking bone metastases. She also had early signs of HPT that were overlooked, leading to a delay in diagnosis. This report emphasizes the importance of considering PHPT in diagnosis of patients with bone symptoms, especially multiple lytic bone lesions.

2. Case presentation

A 35-year-old woman presented to a local hospital with a six-month history of persistent iliac bone pain. The pain had increased

gradually and reached VAS 8/10, resulting in her needing assistance to walk. Her medical history showed that she had received extracorporeal shock wave lithotripsy (ESWL) for bilateral kidney stones two years previously and had suffered a left tibia fracture caused by a minor traffic accident one year previously. She had no abnormality in drug history, family history and psychosocial history. On physical examination, a 1 × 2 cm mass was found at the lower pole of the left lobe of the thyroid gland.

Neck ultrasound showed a 18 × 23 mm hypoechoic parathyroid mass with inner calcification next to the lower pole of the left thyroid lobe. Screening for primary cancer in other sites and multiple myeloma were negative. Because of parathyroid tumor, the laboratory test was evaluated.

Laboratory test showed hypercalcemia (total calcium: 3.57 mmol/l, normal range: 2.15–2.55 mmol/l) and hypophosphatemia (0.51 mmol/l, normal range: 0.81–1.45 mmol/l). Intact PTH was 1497.4 pg/ml (normal range: 15–68.3 pg/ml) and alkaline phosphatase (ALP) was 339 IU/l (normal range, 35–104 IU/l). FT3, FT4, FSH, liver function and kidney function tests were within normal limits.

A pelvic MRI scan showed multiple osteolytic lesions in the iliac bone and 1/3 upper left femur. There was increased radio-tracer uptake in the skull, pelvis, bilateral femur and tibias with 99mTcMDP skeletal scintigraphy. Abdominal ultrasound identified small bilateral kidney stones (Figs. 1–3).

All of these results led us to diagnose the patient with parathyroid carcinoma with multiple bone metastases, differentiating adenoma and brown tumor. The patient consented to undergo the proposed operation. The lower portion of the left lobe of the thyroid gland, including the parathyroid gland, was then resected by

* Corresponding author.

E-mail addresses: ngoxuanquy1979@gmail.com (Q.X. Ngo), duyyhn@gmail.com (D.Q. Ngo), tranductoanhmu@gmail.com (T.D. Tran), leduong.hmu@gmail.com (D.T. Le), hoanggiap94.hmu@gmail.com (G.N. Hoang), lequang@hmu.edu.vn (Q.V. Le).

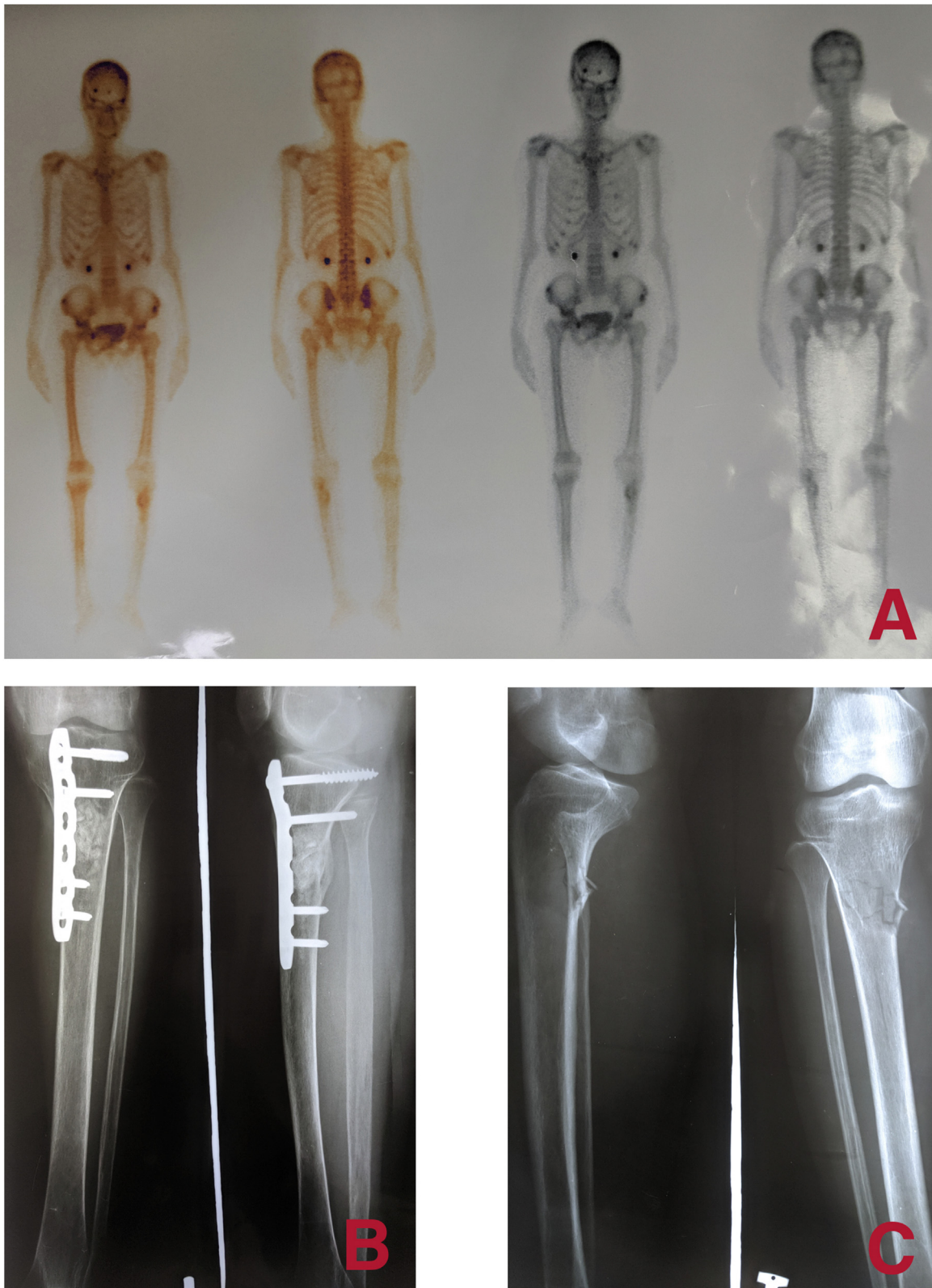


Fig. 1. (A) Whole-body bone scintigraphy: note the increased technetium uptake on bilateral cranium, femur and tibia. (B), (C) Brown tumor on the left femur.

Dr. Quy Xuan Ngo. Pathological results showed parathyroid adenoma. A blood test for baseline PTH was performed at the start of the procedure and the result was 1527 pg/mL. Ten minutes after removal of the tumor, PTH levels decreased to 424 pg/mL, leading us to decide to finish the surgery.

Three days after the operation, the patient experienced numbness and tingling sensations in her fingers and toes. Serum calcium was at 2.06 mmol/l and serum phosphate at 0.81 mmol/l. The patient was diagnosed as having hungry bone syndrome. Acute management involved calcium gluconate intravenous infusion. Her

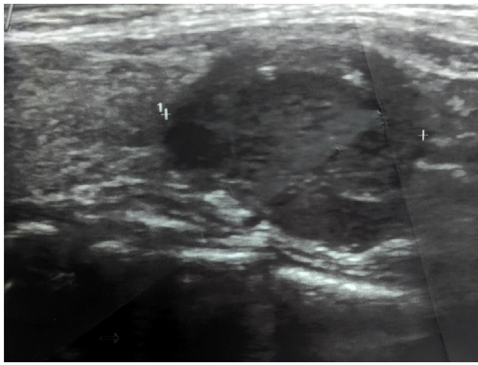


Fig. 2. Neck ultrasound: a 18 × 23 mm hypoechoic mass next to the lower pole of the left thyroid lobe.

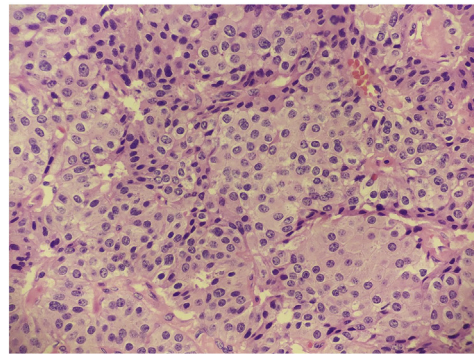
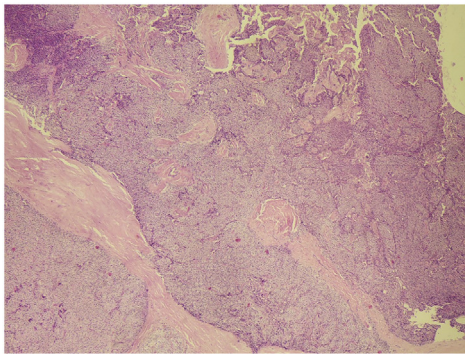
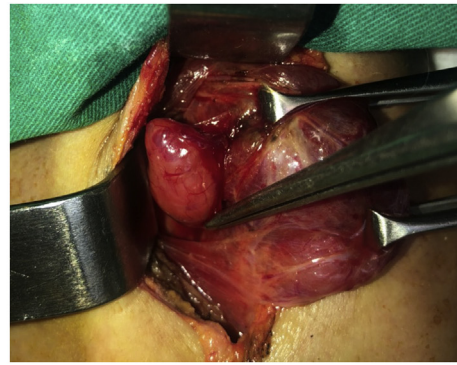


Fig. 3. Pathologic examination suggested an parathyroid adenoma (H.E. ×100, ×400).

symptoms gradually stabilized. The patient was discharged on the fifth day post-operation and prescribed calcium chloride at 1000 mg/day and calcitriol at 1.5 µg/day. The patient has been followed up for three months. PTH and blood calcium level are normal. The imaging manifestation shows no progress in the original brown tumor lesions. The patient has returned to normal life.

3. Clinical discussion

BT represents an extremely rare manifestation of late, uncontrolled HPT with an incidence of 1% in the PHPT group [6]. It result from rapid osteoclastic turnover of bone caused by the abnormal elevation of PTH. The brown coloration is due to hemosiderin deposition [8]. Although the tumors are solitary in most cases, there are a few reports of lesions in multiple sites [9].

In patients presenting with multiple lytic lesions of the bone, the presence of BT should be considered as a differential diagnosis of metastases of a malignant parathyroid. BT and bone metastases are observed in the skull, pelvis, ribs and femur. High levels of Ca and intact PTH in the serum, urolithiasis, and increased radiotracer uptake foci on skeleton scintigraphy are additional similarities. Even though a biopsy is considered the gold standard for diagnosis, it may be inconclusive in many such cases. Thus, differential diagnosis between BT and malignant metastases is very challenging.

The main causes of PHPT are parathyroid adenoma, accounting for 85%, parathyroid hyperplasia, accounting for 10–15%, and carcinoma, accounting for 1–5% [10]. Patients with PHPT often present with symptoms of hypercalcemia, such as bone pain, bone fractures, nephrolithiasis, abdominal groans, psychic moans, and even extreme complications including cardiac arrhythmia or coma.

In developed countries, PHPT is mostly diagnosed by routine biochemical screening without clinical signs suggesting the disease, so the classical manifestations of PHPT are very uncommon [11]. However, in other countries, especially developing countries,

these manifestations are still prevalent, and our case is an example. Although our patient is young, she suffered a left tibia fracture caused by a minor traffic accident and had undergone bilateral kidney stone several years before she was diagnosed with PHPT. While parathyroid hyperplasia typically involves all four glands, adenoma and carcinoma usually appear as a solitary mass [10]. In this patient, a single neck tumor found on physical examination and ultrasound indicated a carcinoma with multiple bone metastases rather than a benign lesion. However, after review of a surgical specimen, the pathology result was adenoma. This suggests that laboratory tests, clinical symptoms and ultrasound are unable to distinguish between malignant and benign parathyroid gland tumors.

Primary treatment of BT caused by PHPT is resection of the hyperfunctioning parathyroid gland, which results in a high recovery rate and a low complications rate [12]. The common complications of parathyroidectomy are principally hematomas, recurrent laryngeal nerve injury, and hypocalcemia [13]. Hypocalcemia poses a significant challenge, leading to increased patient morbidity and healthcare costs [14]. Three days after the operation, our patient displayed symptoms that, on investigation, met the criteria for hungry bone syndrome. The mechanism of this phenomenon is sudden withdrawal of PTH in patients with high bone turnover due to prolonged HPT causing an imbalance between osteoblast-mediated bone formation and osteoclast-mediated bone resorption. This syndrome can be resolved with calcium and vitamin D supplements.

4. Conclusion

This case report emphasizes that brown tumors are an important differential diagnosis in the evaluation of patients presenting with multifocal osteolytic bone lesions, although bone metastases and multiple myeloma still should be considered first. In addition, though rare, a high awareness of the classical manifestation

of PHPT is necessary to avoid a delay in diagnosis, especially in underdeveloped countries. Serum phosphate, serum calcium, and PTH level measurements are helpful diagnostic tools and should be performed routinely in patients with multifocal osteolytic lesions.

Declaration of Competing Interest

None.

Funding

None.

Ethical approval

The study was approved by our research committee, Vietnam National Cancer Hospital, Hanoi, Vietnam.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Author contribution

QuyX.Ngo: Surgeon performed the case.

Duy Q. Ngo, Toan D. Tran: Assisting surgeon.

Duong T. Le: Follow up and post-operative management, wrote manuscript.

Quang V. Le, Giap N. Hoang: Follow up and post-operative management.

Registration of research studies

Not Applicable.

Guarantor

Quang V. Le, M.D.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

We thank Le Van Quang for his contribution to edit the manuscript.

References

- [1] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the SCARE Group, The SCARE 2020 guideline: updating consensus Surgical Case Report (SCARE) guidelines, *Int. J. Surg.* 84 (2020).
- [2] Ö. Can, B. Boynueğri, A.M. Gökçe, E. Özdemir, F. Ferhatoğlu, M. Canbakan, G.M. Şahin, M.I. Titiz, S. Apaydin, Brown tumors: a case report and review of the literature, *Case Rep. Nephrol. Dial.* 6 (2016) 46–52, <http://dx.doi.org/10.1159/000444703>.
- [3] A. Panagopoulos, I. Tatani, H.P. Kourea, Z.T. Kokkalis, K. Panagopoulos, P. Megas, Osteolytic lesions (brown tumors) of primary hyperparathyroidism misdiagnosed as multifocal giant cell tumor of the distal ulna and radius: a case report, *J. Med. Case Rep.* 12 (2018) 176, <http://dx.doi.org/10.1186/s13256-018-1723-y>.
- [4] A.F. Jacobson, P.C. Stomper, M.S. Jochelson, D.M. Ascoli, I.C. Henderson, W.D. Kaplan, Association between number and sites of new bone scan abnormalities and presence of skeletal metastases in patients with breast cancer, *J. Nucl. Med.* 31 (1990) 387–392.
- [5] L.D. Rybak, D.I. Rosenthal, Radiological imaging for the diagnosis of bone metastases, *Q. J. Nucl. Med.* 45 (2001) 53–64.
- [6] J.P. Bilezikian, S.J. Silverberg, E. Shane, M. Parisien, D.W. Dempster, Characterization and evaluation of asymptomatic primary hyperparathyroidism, *J. Bone Miner. Res.* 6 (Suppl 2) (1991) S85–89, <http://dx.doi.org/10.1002/jbmr.5650061419>, discussion S121–124.
- [7] F. Tarello, S. Ottone, P.P. De Giovanni, S. Berrone, [Brown tumor of the jaws], *Minerva Stomatol.* 45 (1996) 465–470.
- [8] F. Selvi, S. Cakarar, R. Tanakol, S. Guler, C. Keskin, Brown tumour of the maxilla and mandible: a rare complication of tertiary hyperparathyroidism, *Dentomaxillofacial Radiol.* 38 (2009) 53–58, <http://dx.doi.org/10.1259/dmfr/81694583>.
- [9] D.J.T. Dagang, J.B. Gutierrez, M.A.S. Sandoval, F.L. Lantion-Ang, Multiple brown tumours from parathyroid carcinoma, *BMJ Case Rep.* (2016), <http://dx.doi.org/10.1136/bcr-2016-215961>, bcr2016215961.
- [10] J.A. Wieneke, A. Smith, Parathyroid adenoma, *Head Neck Pathol.* 2 (2008) 305–308, <http://dx.doi.org/10.1007/s12105-008-0088-8>.
- [11] H. Heath, Clinical spectrum of primary hyperparathyroidism: evolution with changes in medical practice and technology, *J. Bone Miner. Res.* 6 (2009) S63–S70, <http://dx.doi.org/10.1002/jbmr.5650061415>.
- [12] M. Quiriny, M. Moreau, J. Alexiou, G. Andry, Parathyroidectomy in primary hyperparathyroidism: retrospective study of 167 patients, experience in Jules Bordet Institute, *Acta Chir. Belg.* 114 (2014) 118–124.
- [13] B. Van Udelsman, R. Udelsman, Surgery in primary hyperparathyroidism: extensive personal experience, *J. Clin. Densitom.* 16 (2013) 54–59, <http://dx.doi.org/10.1016/j.jocd.2012.11.007>.
- [14] S.M. Kidwai, A.K. Parasher, Y.W. Ho, M.S. Teng, E.M. Genden, Risk stratification for outpatient parathyroidectomy and predictors of postoperative complications, *Am. J. Otolaryngol.* 38 (2017) 26–30, <http://dx.doi.org/10.1016/j.amjoto.2016.09.006>.

Open Access

This article is published Open Access at [sciencedirect.com](https://www.sciencedirect.com). It is distributed under the [IJSCR Supplemental terms and conditions](#), which permits unrestricted non commercial use, distribution, and reproduction in any medium, provided the original authors and source are credited.